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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/086,745 | 02/28/2002 | Gary de Jong | 24601-416C | 8781 |

20985 7590 01/06/2005

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EXAMINER

LAMBERTSON, DAVID A

| ART UNIT | PAPER NUMBER |
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1636

DATE MAILED: 01/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/086,745

Applicant(s)

DE JONG ET AL.

Examiner

David A. Lambertson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 December 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 17-22, 31, 33 and 35-41 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 18-22, 40 and 41 is/are allowed.
- 6) ☒ Claim(s) 17, 31 and 33 is/are rejected.
- 7) ☒ Claim(s) 35-39 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Receipt is acknowledged of a reply to the previous Office Action, filed December 2, 2004.

Claims 17-22, 31, 33 and 35-41 are pending and under consideration in the instant application. Any rejection of record in the previous Office Action, mailed July 2, 2004, that is not addressed in this action has been withdrawn.

Applicant's arguments filed December 2, 2004, with respect to the rejection(s) of claim(s) 17, 31 and 33 under 35 USC 102(b) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made.

Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 17, 31 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nolan *et al.* (as cited in the previous Office Action; see entire document; henceforth Nolan) in view of Neves *et al.* (as cited previously as IDS reference#2; see entire document; henceforth Neves).

Nolan teaches a method and apparatus that employ fluorescence activated cell sorting (FACS) to verify the delivery of at least one chromosome into a host cell of interest (see for example page 5, lines 10-20). Nolan defines a chromosome as on the order of 1-10 mega bases (see for example page 8, lines 21-22), thereby meeting the limitation of a "large nucleic acid" as defined by the instant specification. The method taught by Nolan indicates that it is preferred that the chromosome be fluorescently labeled, and then detected using high-speed fluorimetry (see for example pages 9-10, the bridging paragraph). Nolan further indicates that a host cell of interest includes fibroblasts and parenchyma stem cells (see for example page 8, lines 28-29), thereby meeting the limitations of dependent claim 31. It is also clear from the teachings of Nolan that the number of cells are determined following FACS analysis, as when the cells are sorted a histogram is displayed indicating the quantity of cells possessing the fluorescent property being detected (see for example page 1-2, the bridging paragraph, especially lines 5-7 on page 2).

Although Nolan specifically states that it is preferred that the chromosome used in their method be fluorescently labeled, Nolan does not specifically teaching fluorescently labeling the chromosome prior to delivering it into the cell.

Neves teaches a method for the covalent labeling of DNA with a fluorescent label (see for example the Abstract and page 52, the second and third full paragraphs) while maintaining the structural integrity of the DNA (see for example page 51, bridging paragraph). Neves further teaches transfecting the fluorescently labeled DNA into the NIH 37-3 and CV-1 transformed cell lines using a cationic lipid transfection method (see for example the paragraph bridging the left and right columns of page 52), and subsequently determining the efficiency of transfection of the

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fluorescently labeled DNA into the cell by fluorescence microscopy (see for example Figures 3 and 4, and their respective legends, and the paragraph bridging the left and right columns of page 53). Neves further states that this method represents a significant advantage for the labeling of DNA, whereby the transcriptional inactivation associated with covalently coupling ligands to DNA is not encountered (see for example page 54, right column, third full paragraph).

It would have been obvious to combine the teachings of Nolan with those of Neves because both involve the fluorescent labeling of a nucleic acid, and the detection of said nucleic acid following its transfection into a host cell using fluorimetric methods; thus the teachings are directly related to each other. Although Nolan does not specifically teach the labeling of a nucleic acid prior to its transfection into a cell, Nolan clearly anticipates using a fluorescently labeled chromosome, and Neves teaches a straightforward method for fluorescently labeling DNA (see for example pages 9-10, the bridging paragraph of Nolan). The ordinary skilled artisan would have been motivated to combine the teachings of Nolan and Neves in order to avoid the transcriptional inactivation of DNA associated with labeling DNA with a ligand, which can be avoided by using the fluorescent labeling technique taught by Neves (see for example page 54, right column, third full paragraph of Neves). Because both teachings involve the labeling of DNA with a fluorescent label, there is no reason to expect that one of ordinary skill in the art could not fluorescently label a chromosome using the method taught by Neves, in order to detect the transfection of a fluorescently labeled chromosome into a host cell, as taught by Nolan. Thus, absent evidence to the contrary (i.e., indicating that a chromosome could not be labeled by the method taught by Neves), the ordinary skilled artisan would have had a high expectation of success when fluorescently labeling a chromosome using the method taught by

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Neves, for the purpose of detecting the transfection of a chromosome in a host cell (i.e., the method taught by Nolan).

Response to Applicant's Arguments

Although Applicant's arguments are directed to a different rejection, the Office will address a few arguments made in the traversal as it relates to the instant rejection. Applicant presents the following traversal:

1. Applicant argues that Nolan does not teach the fluorescent labeling of a nucleic acid *prior* to its introduction into a host cell. Rather, Nolan only discloses *one* method, whereby the chromosome is fluorescently labeled *subsequent* to its transfection into a cell (see for example pages 6-7 of Applicant's response).
2. In the previous rejection, the Office asserted that Nolan merely recites that it is "preferred" that the chromosome detected in their method be "fluorescently labeled," and that there was nothing in the teachings of Nolan that limited the fluorescent-labeling to only after the chromosome is introduced into a cell. In response, Applicant argued that the disclosure of a genus was not anticipatory of a disclosure of a genus (note: Applicant additionally indicated that they do not acknowledge that Nolan actually discloses a genus) (see for example page 7, last full paragraph).

In response to Applicant's arguments:

1 and 2. In the newly applied rejection, a method for fluorescently labeling nucleic acids prior to their introduction into a cell is supplied along with Nolan. The purpose of this secondary reference is to indicate that methods of fluorescently labeling DNA prior to its introduction into a

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cell were well known in the art prior to the filing of the instant application. Nolan clearly contemplates using a fluorescently labeled DNA molecule (i.e., a chromosome) in their method; furthermore there is nothing in the teachings of Nolan that limits it to labeling post-transfection. The argument that Nolan only indicates a single example does not mean that other methods would not be clearly contemplated by the teachings of Nolan (e.g., in the instant case, the fluorescent labeling of a chromosome prior to its introduction into a host cell). Instead, the ordinary skilled artisan, knowing that Nolan prefers the use of fluorescently labeled DNA, and knowing that there are efficient methods of fluorescently labeling DNA prior to its introduction of host cells, would have obviously labeled the chromosome of Nolan using the method taught by Neves with a high expectation of success, thus arriving at the instant invention.

In conclusion, although Applicant's arguments are sufficient to overcome the rejection of claims 17, 31 and 33 in view of Nolan alone, they are not found convincing in view of the obvious combination of Neves and Nolan. As such, the new rejection has been made.

Allowable Subject Matter

Claims 18-22, 40 and 41 are allowed.

Claims 35-39 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David A. Lambertson, Ph.D.
AU 1636



JAMES KETTER
PRIMARY EXAMINER